In the Claims:

1. (Currently amended) A method of treating prostate cancer in a human comprising administering to the human a therapeutically effective amount of an antibody which binds ErbB2 and blocks ligand activation of an ErbB receptor substantially more effectively than humanized monoclonal antibody ~~4D5~~ huMAb4D5-8 (HERCEPTIN®).

2. (Currently amended) The method of claim 1 wherein the antibody blocks binding of monoclonal antibody 2C4 (ATCC HB12697) to ErbB2.

3. (Original) The method of claim 1 wherein the antibody blocks TGF-α activation of mitogen-activated protein kinase (MAPK).

4. (Earlier presented) The method of claim 1 wherein the antibody blocks formation of an ErbB hetero-oligomer.

5. (Currently amended) The method of claim 1 wherein the antibody comprises monoclonal antibody 2C4 (ATCC HB12697) or a humanized form thereof ~~2C4~~.

6. (Original) The method of claim 1 wherein the antibody is an antibody fragment.

7. (Original) The method of claim 6 wherein the antibody fragment is a Fab fragment.

8. (Original) The method of claim 1 wherein the antibody is not conjugated with a cytotoxic agent.

9. (Original) The method of claim 6 wherein the antibody fragment is not conjugated with a cytotoxic agent.

10.-21. (Canceled)

22. (Currently amended) A method of treating prostate cancer in a human comprising administering to the human a therapeutically effective amount of an antibody which binds ErbB2, blocks ligand activation of an ErbB receptor, blocks binding of monoclonal antibody 2C4 (ATCC HB12697) to ErbB2, and blocks TGF-α activation of mitogen activated protein kinase (MAPK).

23. (Currently amended) The method of claim 22 wherein the antibody comprises monoclonal antibody 2C4 (ATCC HB12697) or a humanized form thereof ~~2C4~~.

24. (Earlier presented) The method of claim 22 wherein the antibody is an antibody fragment.

25. (Earlier presented) The method of claim 24 wherein the antibody fragment is a Fab fragment.

26. (Earlier presented) The method of claim 22 wherein the antibody fragment is not conjugated with a cytotoxic agent.

27. (Earlier presented) The method of claim 24 wherein the antibody fragment is not conjugated with a cytotoxic agent.

28. (Currently amended) A method of treating androgen dependent prostate cancer in a human comprising administering to the human a therapeutically effective amount of an antibody which binds to an ErbB2 epitope bound by monoclonal antibody 2C4 (ATCC HB12697).

29. (Earlier presented) The method of claim 28 which results in an increased prostate specific antigen (PSA) index in the human.

30. (Currently amended) The method of claim 28 wherein the antibody comprises monoclonal antibody 2C4 (ATCC HB12697) or a humanized form thereof ~~2C4~~.

31. (Currently amended) A method of treating androgen independent prostate cancer in a human comprising administering to the human a therapeutically effective amount of an antibody which binds ErbB2 and blocks ligand activation of an ErbB receptor substantially more effectively than humanized monoclonal antibody ~~4D5~~ huMAb4D5-8 (HERCEPTIN®).

Remarks

Claims 1-9 and 22-31 are pending in this application and stand rejected on various grounds. Claims 1, 2, 5, 22, 23, 28, 30, and 31 have been amended. The amendments are of formal nature and should raise no issues of new matter

introduction. Specific support for the recitation of "humanized monoclonal antibody hMAb4D5-8 (HERCEPTIN®)" is at least at page 14, line 34 and in the Examples. The language "monoclonal antibody 2C4 (ATCC HB12697)" is supported at least at page 14, lines 21-3 and page 42, line 36.

Arguments

Applicants note the correction of inventorship, as requested, and the withdrawal of earlier rejections under 35 U.S.C. 112, second and first paragraphs, and under 35 U.S.C. 102(b) over Curnow, Cancer Immunotherapy, Vol. 45, 210-215, 1997.

Claim Rejections Maintained and New Grounds of Rejection

1. Claims 1-9 and 22-31 were rejected under 35 U.S.C. 112, first paragraph for allegedly failing to comply with the written description requirement. There appear to be three grounds for this rejection.

(1) The Examiner finds that the amendment to claim 1 and claim 31 reciting antibodies which block ligand activation of an ErbB receptor "more effectively" than monoclonal antibody 4D5 introduced "new matter" into the specification. The Examiner notes that "the specification only provides support for contemplation of methods where the antibody to be used in the claimed methods blocks ligand activation of an ErbB receptor *substantially* more effectively than monoclonal antibody 4D5." (2) The Examiner asserts that in view of the broad definition of the 4D5 antibody, "it appears that the claimed methods comprise the use of an antibody that may be functionally compared to an antibody that has very little in common with the one antibody that was used in the working examples (Transtuzumab, huMAb4D5-8)." This leads to the conclusion that "the examples in the specification are not representative of the full scope of the claims."

(3) Third, the Examiner finds that "antibody 2C4 without the reference ATCC number appears to refer to almost any antibody that might bind to Her-2," and is therefore not adequately described.

All grounds of rejection are respectfully traversed. Claims 1 and 31, as currently amended, recite that the antibody used in the claimed method blocks ligand activation "substantially more effectively than humanized monoclonal antibody huMAb4D5-8 (HERCEPTIN®)." In addition, all references in the claims to monoclonal antibody 2C4 have been supplemented to include the recitation of deposit number ATCC HB12697. In view of these amendments, the Examiner is respectfully request to withdraw the present rejection.

2. Claims 1-9, 22-28, 30 and 31 were rejected under 35 U.S.C. 102(e) as allegedly being anticipated by Ross I (U.S. Pre-Grant Publication 2002/0076695; published June 20, 2002).

Ross I allegedly teaches methods for the treatment of prostate cancer by administration of anti-HER2 antibodies, specifically HERCEPTIN®. The rejection appears to be based on the broad definitions provided in the specification for monoclonal antibody 4D5 and reference antibody 2C4, which include antibodies comprising derivatives of the referenced antibodies. This, in the Examiner's reading, meant that the original recitation in the claims of an antibody which binds ErbB2 and blocks ligand activation of an ErbB receptor more effectively than monoclonal antibody 4D5 did not limit the claimed invention. Therefore, the treatment of prostate cancer with any anti-ErbB2 antibody, including the antibodies of Ross I, were found to be within the scope of the claims.

Without acquiescing to the rejection or the Examiner's reading of the claims rejected, the claims now clearly recite that the claimed method uses antibodies that block ligand activation of an ErbB receptor substantially more effectively than humanized monoclonal antibody huMAb4D5-8 (HERCEPTIN®). As Ross I does not disclose, teach or suggest the treatment of prostate cancer by using such antibodies,

the Examiner is respectfully requested to reconsider and withdraw the present rejection.

3. Claims 1-9 and 22-31 were rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Hudziak (U.S. Patent No. 5,725,856) and Ross II (U.S. Patent No. 5,994,071) in view of Sliwkowski (J. Biol. Chem. 269:14661-14665, 1994) or Klapper (Oncogene, 14:1099-2109, 1997) and further in view of Plowman (U.S. Patent No. 5,804,396) or Akita (U.S. Patent No. 5,968,511) or Greene (U.S. Patent No. 6,417,168). Hudziak has been relied on for its teaching of methods of inhibiting the growth of tumor cells by administering to a patient antibodies capable of inhibiting ErbB2 function, and teaching inhibition of the growth of tumor cells that overexpress ErbB2. Ross II has been cited for its teaching that prostate cancer cells over-express ErbB2 and that expression of ErbB2 is associated with poor prognosis. Sliwkowski has been relied on for its teaching that monoclonal antibody 2C4 inhibits the activation of ErbB2 by heregulin. Klapper has been cited for its teaching of antibodies that bind to ErbB2 and inhibit interaction of ErbB2 with other ErbB receptors. Sliwkowski has been cited for its disclosure of monoclonal antibody 2C4, which inhibits the activation of ErbB2 by heregulin. Plowman, Akita and Greene have been included to allegedly demonstrate that the prior art recognized that the inhibition of ErbB2 oligomerization with other ErbB receptors is a therapeutic target for the treatment of cancer.

According to the rejection, at the time the invention was made it would have been obvious to one of ordinary skill in the art to have used the antibodies of either Sliwkowski or Klapper in the method of Hudziak or Ross II for the treatment of prostate cancer. In addition, the Examiner finds motivation to use antibodies inhibiting ligand activation of an ErbB receptor "in view of the fact that the art recognized that ErbB2 was activated by the formation of heterodimers and that ErbB2 activation plays a role in the growth of prostate cancer cells."

Although it is not specifically stated, this rejection, again, appears to be based on a broad reading of the meaning of monoclonal antibodies 4D5 and 2C4. The

claims as currently amended clearly recite that the claimed method uses antibodies that block ligand activation of an ErbB receptor substantially more effectively than humanized monoclonal antibody huMAb4D5-8 (HERCEPTIN®). Even if one assumes arguendo, but without admission, that the purported combination of references is proper, the references provide the teaching relied upon, and their combination results in the teaching asserted in support of the rejection, the cited combination has no suggestion whatsoever that one could provide antibodies that bind ErbB2 and block ligand activation of an ErbB receptor in a human subject substantially more effectively than humanized monoclonal antibody huMAb4D5-8 (HERCEPTIN®). Accordingly, the Examiner is respectfully requested to reconsider and withdraw the present rejection.

4. Claims 1-9 and 22-31 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 42, 45, 55 (Applicants believe claim 56 was intended) and 66 of copending Application No. 09/705,579.

This rejection was based on the inclusion of claims in the '579 application drawn to methods for treatment of prostate cancer, comprising administering an antibody such as monoclonal antibody 7F3. However, the claims of the '579 application were recently amended such that claims to therapy with an antibody that binds to 7F3's epitope were cancelled, thus rendering the rejection moot. Reconsideration and withdrawal of the rejection is respectfully requested.

5. Claims 1-9 and 22-31 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting over claims 1, 2, 4-9, 16-22, 24-27, and 60-63 of copending Application No. 09/600,812 (Applicants believe USSN 09/602,812 is intended).

Applicants respectfully traverse the rejection.

The Examiner asserts in formulating the rejection that a "preferred embodiment described in the specification is prostate cancer." However, for obviousness-type

double patenting rejection, the relevant comparison in between the inventions claimed, rather than that which might be described in the specification (see, e.g. M.P.E.P., Section 1504.06: "*Double patenting rejections are based on a comparison of the claims in a patent and an application or between two applications* . . ."). Claims 1, 2, 4-9, 16-22, 24-27, and 60-63 of the '812 application are not directed to therapy of prostate cancer, much less androgen independent prostate cancer or androgen dependent prostate cancer, as are the claims of the present application. Indeed, the PTO has held in the '812 application that therapy of different species of cancer represents patentably distinct species because "Different types of cancers have different mechanisms of action, and require distinct treatment protocols" (Restriction Requirement dated 10/02/01, Paper # 7 in the '812 application, page 5). Hence, since the present claims concern therapy of prostate cancer, androgen independent prostate cancer, or androgen dependent prostate cancer, and the claims of the '812 application do not refer to therapy of such cancers, Applicants submit that the rejection should be reconsidered and withdrawn.

6. Claims 1-9 and 22-31 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 28-40 and 42-62 of copending Application No. 08/948,149. Applicants respectfully traverse this rejection.

As noted above in Section 5, the Patent Office is of the view that therapy of a selected species of cancer is patentably distinct. The rejection appears to be based on the teaching in the '149 application "that prostate cancer is a target of the claimed methods." However, as noted above, the relevant comparison is the claims of the two different applications, rather than that which is described in the specification. Whereas the present claims are directed to therapy of prostate cancer, androgen independent prostate cancer, or androgen dependent prostate cancer, none of claims 28-40 and 42-62 of the '149 application are directed to prostate cancer therapy.

Reconsideration and withdrawal of the rejection is respectfully requested in view of the above.

All claims pending in this application are believed to be in prima facie condition for allowance, and an issuance of a Notice of Allowance is respectfully solicited.

Sincerely,

Date: March 24, 2004

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